UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Wednesday, April 12, 2006

MEMORANDUM

Subject: Acute Toxicity Review for EPA Reg. No.: 4822-LUO/ PHAB
DP Barcode: D326613

To: Adam Heyward, PM 34/ Killian Swift
Regulatory Management Branch
Antimicrobials Division (7510C)

From: Ian Blackwell, Biologist
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510C)

Through: Karen Hicks, Team Leader
Chemistry and Toxicology Team
Product Science Branch
Antimicrobials Division (7510C)

4/12/06

Michele E. Wingfield, Chief
Product Science Branch
Antimicrobials Division (7510C)

Applicant: S.C. Johnson & Son, Inc.

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
L-Lactic Acid	0.18
Other Ingredient(s):	99.82
Total:	100.00%

I BACKGROUND: S.C. Johnson and Son have submitted a complete set of six acute toxicity studies to support the registration of their product. "PHAB". These studies were conducted by Charles River Laboratories, Inc. (formerly Springborn Laboratories).

II RECOMMENDATIONS: PSB findings are:

1 Each of the six studies is acceptable.

2 The dermal sensitization study referenced a positive control study using α-HCA as the control material. This study was not conducted within six months of the sensitization study of the registration product; thus, it is not acceptable. However, the first referenced positive control study (this study used two positive control studies), using DNCB, was conducted within the proper time frame and is acceptable.

The acute toxicity profile for File Symbol 4822-LUO is currently:

Study	MRID Number	Toxicity Category	Status
acute oral toxicity	467504-03	IV	Acceptable
acute dermal toxicity	467504-04	IV	Acceptable
acute inhalation toxicity	467504-05	IV	Acceptable
primary eye irritation	467504-06	IV	Acceptable
primary skin irritation	467504-07	IV	Acceptable
dermal sensitization	467504-08	Nonsensitizer	Acceptable

III LABELING:

Due to the acute toxicity profile of this product, no precautionary labeling is required.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§ 81-1, 870.1100)

Product Manager: 34 **Reviewer**: I. Blackwell
MRID No.: 467504-03 **Study Completion Date**: 12/2/2005
Lab Study No.: RZB00053
Testing Laboratory: Charles River Laboratories, Inc.
Authors: Dawn D. Rodabaugh, B.S.

Quality Assurance (40 CFR §160.12): Included

Test Material: PHAB 1, "clear, colorless liquid"

Species: Hsd: Sprague-Dawley SD rats
Age: 9-10 weeks (all females)
Weight: 183-203 g
Source: Harlan Sprague Dawley, Inc.

Conclusion:

1. **LD_{50} (mg/kg):** **Males = (not tested)**
   Females > 5,000 mg/kg
   Combined =
2. **The estimated LD_{50} is greater than 5,000 mg/kg b.w.**
3. **Tox. Category**: IV **Classification**: Acceptable

Procedure (Deviations from §81-1): None

Results:

Dosage (mg/kg)	(Number Deaths/Number Tested)		
	Males	Females	Combined
5,000	---	0/3	N/A

Observations: No clinical abnormalities were observed.

Gross Necropsy: "All tissues within normal limits."

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2, 870.1200)

Product Manager: 34
MRID No.: 467504-04

Reviewer: Ian Blackwell
Study Completion Date: 12/2/05
Lab Study No.: RZB00054

Testing Laboratory: Charles River Laboratories, Inc.
Author: Dawn D. Rodabaugh, B.S.
Quality Assurance (40 CFR §160.12): Included

Test Material: PHAB 1, "clear, colorless liquid"

Species: New Zealand White rabbit
Weight: males= 2.5-2.8 kg; females= 2.7-2.9 kg **Age**: 12 weeks
Source: Myrtle's Rabbitry

Summary:

1. **LD_{50} (mg/kg)**: **Males** > 5,000
   Females > 5,000
   Combined > 5,000

2. **The estimated LD_{50} is greater than 5,000 mg/kg of b.w.**

3. **Tox. Category**: IV **Classification**: Acceptable

Procedure (Deviation From §81-2): None

Results:

Reported Mortality

DOSAGE (mg/kg)	(NUMBER DEATHS/NUMBER TESTED)		
	Males	Females	Combined
5,000	0/5	0/5	0/10

Observations: Soft stools, rough coat and dermal irritation.

Gross Necropsy Findings: There were no gross internal findings.

DATA REVIEW FOR ACUTE INHALATION TOXICITY (§81-3, 870.1300)

Product Manager: 34
MRID No.: 467504-05

Reviewer: I. Blackwell
Study Completion Date: 12/9/05
Lab Study No.: RZB00055

Testing Laboratory: Charles River Laboratories, Inc.
Author: Dawn D. Rodabaugh, B.S.

Quality Assurance (40 CFR §160.12): Included

Test Material: PHAB 1, "clear, colorless liquid"
Concentration: 5.59 mg/L (analytically determined)

Species: Sprague Dawley rats
Weight: males= 302-333 g; females= 207-224 g
Age: 9 weeks
Source: Harlan Sprague Dawley, Inc.

Summary:

1. **LC_{50} (mg/L):** **Males** > 5.59 mg/L
   Females > 5.59 mg/L
   Combined > 5.59 mg/L

2. **The estimated LC_{50} is greater than 5.59 mg/L of air.**

3. **MMAD**: 4.1 μm

4. **Tox. Category**: IV **Classification**: Acceptable

Procedure (Deviation From §81-3): None

Results:

Table 1 **Reported Mortality**

Exposure Concentration	(NUMBER DEATHS/NUMBER TESTED)		
	Males	Females	Combined
5.59 mg/L	0/5	0/5	0/10

Table 2

Chamber Atmosphere			
Dose Level	MMAD	GSD	Particles <4.0 μm
5.59 mg/L	4.1 μm	2.49 μm	52%

Table 3

Chamber Environment	
Chamber Volume	10 L
Airflow	54 LPM
Temperature	73.0-73.5° C
Relative Humidity	72.0-74.3%
Oxygen Content	20.9%

Clinical Observations: Congested breathing, dark material around the facial area weight loss in 3 females.

Gross Necropsy Findings: Thinned area of diaphragm (1 male) and thymic foci (1 male).

DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (§81-4, 870.2400)

Product Manager: 34
Reviewer: Ian Blackwell
MRID No.: 467504-06
Study Completion Date: 12/2/05
Lab Study No.: RZB00056
Testing Laboratory: Charles River Laboratories, Inc.
Author(s): Dawn D. Rodabaugh, B.S.

Quality Assurance (40 CFR §160.12):

Test Material: PHAB 1, "clear, colorless liquid"
Dosage: 0.1 mL

Species: New Zealand White rabbits
Sex: 3 males
Weight: 2.469 – 2.554 kg
Age: approx. 12 weeks
Source: Myrtle's Rabbitry

Summary:

1. **Toxicity Category**: IV
2. **Classification**: Acceptable

Procedure (Deviations From §81-4): None

Results:

Observations	(number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
Corneal Opacity	0/3	0/3	0/3	0/3	---	---	---	---
Iritis	2/3	0/3	0/3	0/3	---	---	---	---
Conjunctivae								
Redness	1/3	0/3	0/3	0/3	---	---	---	---
Chemosis	1/3	0/3	0/3	0/3	---	---	---	---
Discharge	0/3	0/3	0/3	0/3	---	---	---	---

--- = no observations at this point

DATA REVIEW FOR SKIN IRRITATION TESTING (§81-5, 870.2500)

Product Manager: 34
MRID No.: 467504-07

Reviewer: Ian Blackwell
Study Completion Date: 12/2/5
Lab Study No.: RZB00057

Testing Laboratory: Charles River Laboratories, Inc.
Author: Dawn D. Rodabaugh, B.S.

Quality Assurance (40 CFR §160.12): Included

Test Material: PHAB 1, "clear, colorless liquid"
Dosage: 0.5 mL
Species: New Zealand White rabbits
Age: adult
Sex: 3 males
Weight: 2.377 – 2.785 kg
Source: Myrtle's Rabbitry

Summary:

1. **Toxicity Category**: IV

2. **Classification**: Acceptable

Procedure (Deviations From §81-5): None

Results: Very slight erythema was observed in 2/3 treated animals one hour after the exposure. Twenty-four hours after treatment, no dermal irritation was observed in any of the 3 animals.

Special Comments: Irritation due to the adhesive tape was observed.

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (§81-6, 870.2600)

Product Manager: 34
MRID No.: 467504-08
Reviewer: I. Blackwell
Study Completion Date: 12/2/5
Lab Study No.: RZB00058
Testing Laboratory: Charles River Laboratories, Inc.
Author: Dawn D. Rodabaugh, B.S.

Quality Assurance (40 CFR §160.12): Included

Test Material: PHAB 1, "clear, colorless liquid"
Positive Control Material: 1-Chloro-2,4-dinitrobenzene (DNCB), and, α-Hexylcinnamaldehyde (α- HCA)

Species: Hartley-derived guinea pig
Weight: 310 – 395 g
Age: young adult
Source: Hilltop Lab Animals, Inc.

Method: Modified Buehler Design

Summary:

1. **This Product is not a dermal sensitizer.**

2. **Classification**:

Procedure (Deviation From §81-6):

- This study referenced **two** positive control studies.
- The α-HCA study was not conducted within six months of the main test study.

Procedure:

Test:
Induction: Test animals were induced using 0.3 mL of undiluted (100%) test material in a 25mm Hilltop Chamber. The animals were dosed in this manner on Days 0, 7 and 14 of the study, for a total of 3 induction doses.

Challenge: On Day 27 of the study, the test material-induced animals were challenged with 0.3 mL of undiluted test material.

Positive Control:

DNCB Induction: The DNCB positive control animals were induced in the same manner as the test subjects, except that they received 0.3 mL of 0.1% DNCB in ethanol/acetone in a Hilltop Chamber.

α-HCA Induction: The α-HCA positive control animals were induced in the same manner as the test material-treated animals, except that they received 0.3 mL of 5% HCA in ethanol.

DNCB Challenge: The DNCB positive control animals were challenged in the same manner as the test subjects, except that they received 0.3 mL of 0.1% and 0.05% DNCB in ethanol/acetone in a 25 mm Hilltop Chamber.

α-HCA Challenge: The HCA positive control animals were challenged in the same manner as the test subjects, except that they received 0.3 mL of 2.5% and 1.0% DNCB in ethanol/acetone in a 25 mm Hilltop Chamber.

Results:

Test Material-Treated Group: Twenty-four hours after induction treatment #1, 1/20 test material-induced animals displayed slight, patchy erythema. Twenty-four hours after induction treatments 2 and 3, no irritation was observed in any of the 20 test material-inducted animals.

DNCB Group: Twenty-four hours after the first induction treatment (#1), 12/20 positive control animals had slight, patchy erythema and 20/20 had yellow staining of the test site. Twenty-four hours after induction treatment #2, 5/20 had moderate confluent erythema, 15/20 had slight confluent or moderate patchy erythema, 18/20 had slight or very slight edema, and, 20/20 had yellow staining of the test site from the HCA. Twenty-four hours after induction #3, 7/20 had moderate confluent erythema, 12/20 had slight patchy erythema, 1/20 had slight patchy erythema, 20/20 still had staining of the test site, 20/20 had slight or very slight edema, 8/20 had superficial lightening of the skin, 4/20 had blanching, and 17/20 had desquamation.

Twenty-four hours after challenge, 8/20 positive control animals displayed moderate erythema, 7/20 slight confluent or moderate patchy erythema, 12/20 had edema, 9/20 had superficial lightening, and 20/20 had test material staining from the positive control. At this same point in the study, 3/10 naïve control animals displayed slight patchy erythema, and, 20/20 had test material staining.

α-HCA Group: This positive control study was not conducted within six months of the main test of Phab-1; therefore, it is not acceptable. However, the DNCB study is acceptable and supports the main study.